What is claimed is:

1. A method for engineering a spatially conserved catalytic motif into a recipient polypeptide that binds a target, the method comprising:

a) obtaining a spatial relationship for the amino acid residues of a spatially conserved catalytic motif;

b) identifying a set of amino acid residues in the recipient polypeptide, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the catalytic motif, and wherein the recipient polypeptide binds to a target that is an extracellular signaling molecule with a K_D of 10^{-6}M or less; and

c) substituting said set of residues in said recipient polypeptide with a set of amino acid residues making up said catalytic motif;

thereby engineering a catalytic motif into a recipient polypeptide that binds to an extracellular signaling molecule.

2. A method for engineering a spatially conserved target binding motif into a recipient polypeptide that catalytically modifies a target, the method comprising:

a) obtaining a spatial relationship for the amino acid residues of a spatially conserved target binding motif, wherein the target binding motif mediates binding to a target that is an extracellular signaling molecule with a K_D of 10^{-6}M or less; and

b) identifying a set of amino acid residues in a recipient polypeptide, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the target binding motif; and

c) substituting said set of residues in said recipient polypeptide with a set of amino acid residues making up said target binding motif;

thereby engineering a target binding motif that binds to an extracellular signaling molecule target into a recipient polypeptide that catalytically modifies the target.

3. The method of claim 1, wherein the targeted extracellular signaling molecule is an inflammatory cytokine.

4. The method of claim 1, wherein the targeted extracellular signaling molecule is TNF-α.

5. The method of claim 1, wherein the recipient polypeptide is selected from among: a binding portion of an anti- TNF-α antibody, a soluble ligand binding portion of a TNF-α receptor and a TNF-α polypeptide.

6. The method of claim 1, wherein the catalytic motif catalyzes proteolysis of the target.

7. The method of claim 1, wherein the catalytic motif comprises a serine protease triad.

8. The method of claim 1, wherein said set of residues identified in said recipient polypeptide are less than about 10Å away from a target binding site.

9. The method of claim 1, further comprising constructing a model of said recipient polypeptide containing said set of substituted residues in silico and determining the existence of atomic clashes between atoms in said model.

10. The method of claim 9, wherein the model is rejected if atomic clashes are present between atoms in said model.

11. The method of claim 1, further comprising constructing a model of said recipient polypeptide containing said set of substituted residues in silico and comparing the polypeptide backbone of said recipient polypeptide in the presence and absence of said set of substituted residues.

12. The method of claim 11, further comprising determining the root mean squared deviation of α-carbon atoms in said polypeptide backbone in the presence and absence of said set of substituted residues.

13. The method of claim 12, wherein the model is rejected if there is a root mean squared deviation of greater than 2Å between backbone α-carbon atoms.

14. The method of claim 1, wherein said spatially conserved motif comprises a number of amino acid residues selected from the group consisting of 2, 3, 4, 5, 6, 7, and 8.

15. The method of claim 1, wherein identifying said set of amino acid residues in the recipient polypeptide includes modeling the presence of a β-carbon on a glycine residue of the recipient polypeptide.

16. The method of claim 15, wherein said set of residues in said recipient polypeptide comprise a glycine residue.

17. A method for engineering a spatially conserved catalytic motif into a recipient polypeptide that binds a target, the method comprising:

d) obtaining a spatial relationship for the amino acid residues of a spatially conserved catalytic motif;

e) identifying a set of amino acid residues in the recipient polypeptide, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the catalytic motif, and wherein the recipient polypeptide binds to a target that is a receptor for an extracellular signaling molecule with a K_D of 10^{-6}M or less; and

f) substituting said set of residues in said recipient polypeptide with a set of amino acid residues making up said catalytic motif;

thereby engineering a catalytic motif into a recipient polypeptide that binds to a receptor for an extracellular signaling molecule.

18. The method of claim 17, wherein the target is a receptor for TNF-α.

19. The method of claim 17, wherein the recipient polypeptide is a ligand for the receptor.

20. The method of claim 18, wherein the recipient polypeptide is a TNF-α.

21. A method for engineering a spatially conserved motif into a recipient polypeptide, the method comprising:

a) obtaining a spatial relationship for the amino acid residues of a spatially conserved motif;

b) identifying a set of amino acid residues in a recipient polypeptide, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the motif, and wherein identifying said set of amino acid residues in the recipient polypeptide includes modeling the presence of a β-carbon on a glycine residue of the recipient polypeptide; and

c) substituting said set of residues in said recipient polypeptide with a set of amino acid residues making up said motif;

thereby engineering a spatially conserved motif into a recipient polypeptide.

22. The method of claim 21, wherein the recipient polypeptide binds to a target molecule.

23. The method of claim 22, wherein the target molecule is an extracellular signaling molecule is an inflammatory cytokine.

24. The method of claim 23, wherein the extracellular signaling molecule is TNF-α.

25. The method of claim 21, wherein the motif is a catalytic motif.

26. The method of claim 25, wherein the catalytic motif catalyzes proteolysis of the target.

27. The method of claim 26, wherein the catalytic motif comprises a serine protease triad.

28. The method of claim 21, wherein said set of residues identified in said recipient polypeptide are less than about 10Å away from a target binding site.

29. The method of claim 21, further comprising constructing a model of said recipient polypeptide containing said set of substituted residues in silico and determining the existence of atomic clashes between atoms in said model.

30. The method of claim 29, wherein the model is rejected if atomic clashes are present between atoms in said model.

31. The method of claim 21, further comprising constructing a model of said recipient polypeptide containing said set of substituted residues in silico and comparing the polypeptide backbone of said recipient polypeptide in the presence and absence of said set of substituted residues.

32. The method of claim 31, further comprising determining the root mean squared deviation of α-carbon atoms in said polypeptide backbone in the presence and absence of said set of substituted residues.

33. The method of claim 32, wherein the model is rejected if there is a root mean squared deviation of greater than 2Å between backbone α-carbon atoms.

34. The method of claim 21, wherein said spatially conserved motif comprises a number of amino acid residues selected from the group consisting of 2, 3, 4, 5, 6, 7, and 8.

35. The method of claim 21, wherein said set of residues in said recipient polypeptide comprise a glycine residue.

36. A method for engineering a spatially conserved motif into a recipient polypeptide complex, the method comprising:

a) obtaining a spatial relationship for the amino acid residues of a spatially conserved motif;

b) identifying a set of amino acid residues in a recipient polypeptide complex, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the motif, and wherein said set of amino acid residues includes amino acid residues of more than one polypeptide in the recipient polypeptide complex; and

c) substituting said set of residues in said recipient polypeptide complex with a set of amino acid residues making up said motif;

thereby engineering a spatially conserved motif into a recipient polypeptide complex.

37. The method of claim 36, wherein the recipient polypeptide binds to a target molecule.

38. The method of claim 37, wherein the target molecule is an extracellular signaling molecule is an inflammatory cytokine.

39. The method of claim 38, wherein the extracellular signaling molecule is TNF-α.

40. The method of claim 37, wherein the target molecule is a receptor.

41. The method of claim 40, wherein the receptor is a receptor for an extracellular signaling molecule.

42. The method of claim 41, wherein the receptor is a receptor for TNF-α.

43. The method of claim 36, wherein the motif is a catalytic motif.

44. The method of claim 43, wherein the catalytic motif catalyzes proteolysis of a target.

45. The method of claim 44, wherein the catalytic motif comprises a serine protease triad.

46. The method of claim 36, wherein the recipient polypeptide complex is an antibody or a complex comprising an antigen binding portion of an antibody.

47. The method of claim 36, wherein said set of residues identified in said recipient polypeptide complex are less than about 10Å away from a target binding site.

48. The method of claim 36, further comprising constructing a model of said recipient polypeptide complex containing said set of substituted residues in silico and determining the existence of atomic clashes between atoms in said model.

49. The method of claim 48, wherein the model is rejected if atomic clashes are present between atoms in said model.

50. The method of claim 36, further comprising constructing a model of said recipient polypeptide complex containing said set of substituted residues in silico and comparing the polypeptide backbones of said recipient polypeptide complex in the presence and absence of said set of substituted residues.

51. The method of claim 50, further comprising determining the root mean squared deviation of α-carbon atoms in said polypeptide backbones in the presence and absence of said set of substituted residues.

52. The method of claim 36, wherein the model is rejected if there is a root mean squared deviation of greater than 2Å between backbone α-carbon atoms.

53. The method of claim 36, wherein said spatially conserved motif comprises a number of amino acid residues selected from the group consisting of 2, 3, 4, 5, 6, 7, and 8.

54. The method of claim 36, wherein identifying said set of amino acid residues in the recipient polypeptide includes modeling the presence of a β-carbon on a glycine residue of the recipient polypeptide.

55. The method of claim 54, wherein said set of residues in said recipient polypeptide comprise a glycine residue.

56. A method for engineering a spatially conserved partial motif into a target binding recipient polypeptide or polypeptide complex, the method comprising:

a) obtaining a spatially conserved residue geometry for a spatially conserved motif;

b) identifying a set of amino acid residues in a holo-complex comprising the recipient polypeptide or polypeptide complex and the target, wherein said set of residues have a geometric relationship that matches the spatially conserved geometry of the catalytic motif and wherein at least one of said amino acid residues of the set occur in the target;

c) identifying in the set of amino acid residues a subset of amino acid residues that are present on the recipient polypeptide or polypeptide complex;

d) substituting the subset of residues in said recipient polypeptide or polypeptide complex with the corresponding amino acid residues of said motif;

thereby engineering a partial motif into a recipient polypeptide or polypeptide complex such that binding of the engineered recipient polypeptide or polypeptide complex to the target reconstitutes the motif.

57. An engineered polypeptide or polypeptide complex that binds to an extracellular signaling molecule and comprises an engineered spatially conserved catalytic motif which catalytically modifies the extracellular signaling molecule.

58. The engineered polypeptide or polypeptide complex of claim 57, wherein the catalytic motif confers protease activity.

59. The engineered polypeptide or polypeptide complex of claim 58, wherein the catalytic motif comprises a serine protease triad.

60. The engineered polypeptide or polypeptide complex of claim 56, wherein the extracellular signaling molecule is an inflammatory cytokine.

61. The engineered polypeptide or polypeptide complex of claim 60, wherein the extracellular signaling molecule is TNF-α.

62. The engineered polypeptide or polypeptide complex of claim 56, wherein the polypeptide or polypeptide complex into which the catalytic motif has been engineered is selected from among: a soluble receptor that binds the target extracellular signaling molecule, an antibody that binds the target, a portion of an antibody that binds the target and a monomer or multimer of the extracellular signaling molecule.

63. An engineered polypeptide or polypeptide complex that binds to a receptor for an extracellular signaling molecule and comprises an engineered spatially conserved catalytic motif which catalytically modifies the extracellular signaling molecule.

64. The engineered polypeptide or polypeptide complex of claim 63, wherein the catalytic motif confers protease activity.

65. The engineered polypeptide or polypeptide complex of claim 63, wherein the catalytic motif comprises a serine protease triad.

66. The engineered polypeptide or polypeptide complex of claim 63, wherein the receptor is a receptor for an inflammatory cytokine.

67. The engineered polypeptide or polypeptide complex of claim 66, wherein the receptor is a receptor for TNF-α.

68. The engineered polypeptide or polypeptide complex of claim 63, wherein the polypeptide or polypeptide complex into which the catalytic motif has been

engineered is selected from among: an antibody that binds the target, a portion of an antibody that binds the target and a monomer or multimer of the extracellular signaling molecule.

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